```
=> file .nash

=> s (interleukin-22 or il-22) and (muta? or variant)
L1             4 FILE MEDLINE
L2            14 FILE CAPLUS
L3             4 FILE SCISEARCH
L4             2 FILE LIFESCI
L5             2 FILE BIOSIS
L6             3 FILE EMBASE

TOTAL FOR ALL FILES
L7            29 (INTERLEUKIN-22 OR IL-22) AND (MUTA? OR VARIANT)

=> s l7 not 2003-2004/py
TOTAL FOR ALL FILES
L14           14 L7 NOT 2003-2004/PY

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15            4 DUP REM L14 (10 DUPLICATES REMOVED)

=> d ibib abs 1-4

L15  ANSWER 1 OF 4     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2002471904     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 12087100
TITLE:               Interleukin-22 (IL-22
                     ) activates the JAK/STAT, ERK, JNK, and p38 MAP kinase
                     pathways in a rat hepatoma cell line. Pathways that are
                     shared with and distinct from IL-10.
AUTHOR:              Lejeune Diane; Dumoutier Laure; Constantinescu Stefan;
                     Kruijer Wiebe; Schuringa Jan Jacob; Renauld Jean-Christophe
CORPORATE SOURCE:    Ludwig Institute for Cancer Research, Brussels Branch,
                     Experimental Medicine Unit, Universite de Louvain, avenue
                     Hippocrate 74, B-1200 Brussels, Belgium.
SOURCE:              Journal of biological chemistry, (2002 Sep 13) 277 (37)
                     33676-82.
                     Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200212
ENTRY DATE:          Entered STN: 20020918
                     Last Updated on STN: 20030105
                     Entered Medline: 20021203
AB   IL (interleukin)-22 is an IL-10-related cytokine; its
     main biological activity known thus far is the induction of acute phase
     reactants in liver and pancreas. IL-22 signals
     through a receptor that is composed of two chains from the class II
     cytokine receptor family: IL-22R (also called ZcytoR11/CRF2-9) and
     IL-10Rbeta (CRF2-4), which is also involved in IL-10 signaling. In this
     report, we analyzed the signal transduction pathways activated in response
     to IL-22 in a rat hepatoma cell line, H4IIE. We found
     that IL-22 induces activation of JAK1 and Tyk2 but not
     JAK2, as well as phosphorylation of STAT1, STAT3, and STAT5 on tyrosine
     residues, extending the similarities between IL-22 and
     IL-10. However our results unraveled some differences between IL
     -22 and IL-10 signaling. Using antibodies specific for the
     phosphorylated form of MEK1/2, ERK1/2, p90RSK, JNK, and p38 kinase, we
     showed that IL-22 activates the three major MAPK
     pathways. IL-22 also induced serine phosphorylation
     of STAT3 on Ser(727). This effect, which is not shared with IL-10, was
     only marginally affected by MEK1/2 inhibitors, indicating that other
     pathways might be involved. Finally, by overexpressing a STAT3 S727A
     mutant, we showed that serine phosphorylation is required to
     achieve maximum transactivation of a STAT responsive promoter upon
     IL-22 stimulation.

L15  ANSWER 2 OF 4     MEDLINE on STN                    DUPLICATE 2
```

ACCESSION NUMBER: 2002376975 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11970958
TITLE: The conserved helix C region in the superfamily of interferon-gamma /interleukin-10-related cytokines corresponds to a high-affinity binding site for the HSP70 chaperone DnaK.
AUTHOR: Vandenbroeck Koen; Alloza Iraide; Brehmer Dirk; Billiau Alfons; Proost Paul; McFerran Neil; Rudiger Stefan; Walker Brian
CORPORATE SOURCE: Biomolecular Sciences Research Group, McClay Research Centre for Pharmaceutical Sciences, Queen's University of Belfast, United Kingdom.. k.vandenbroeck@qub.ac.uk
SOURCE: Journal of biological chemistry, (2002 Jul 12) 277 (28) 25668-76.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020719
Last Updated on STN: 20030105
Entered Medline: 20020812

AB HSP70 chaperones mediate protein folding by ATP-dependent interaction with short linear peptide segments that are exposed on unfolded proteins. The mode of action of the Escherichia coli homolog DnaK is representative of all HSP70 chaperones, including the endoplasmic reticulum **variant** BiP/GRP78. DnaK has been shown to be effective in assisting refolding of a wide variety of prokaryotic and eukaryotic proteins, including the alpha-helical homodimeric secretory cytokine interferon-gamma (IFN-gamma). We screened solid-phase peptide libraries from human and mouse IFN-gamma to identify DnaK-binding sites. Conserved DnaK-binding sites were identified in the N-terminal half of helix B and in the C-terminal half of helix C, both of which are located at the IFN-gamma dimer interface. Soluble peptides derived from helices B and C bound DnaK with high affinity in competition assays. No DnaK-binding sites were found in the loops connecting the alpha-helices. The helix C DnaK-binding site appears to be conserved in most members of the superfamily of interleukin (IL)-10-related cytokines that comprises, apart from IL-10 and IFN-gamma, a series of recently discovered small secretory proteins, including IL-19, IL-20, **IL-22**/IL-TIF, IL-24/MDA-7 (melanoma differentiation-associated gene), IL-26/AK155, and a number of viral IL-10 homologs. These cytokines belong to a relatively small group of homodimeric proteins with highly interdigitated interfaces that exhibit the strongly hydrophobic character of the interior core of a single-chain folded domain. We propose that binding of DnaK to helix C in the superfamily of IL-10-related cytokines may constitute the hallmark of a novel conserved regulatory mechanism in which HSP70-like chaperones assist in the formation of a hydrophobic dimeric "folding" interface.

L15 ANSWER 3 OF 4 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:806138 SCISEARCH
THE GENUINE ARTICLE: 479FW
TITLE: A novel, soluble homologue of the human IL-10 receptor with preferential expression in placenta
AUTHOR: Gruenberg B H; Schoenemeyer A; Weiss B; Toschi L; Kunz S; Wolk K; Asadullah K; Sabat R (Reprint)
CORPORATE SOURCE: Schering AG, Dept Expt Dermatol, Muellerstr 178, D-13342 Berlin, Germany (Reprint); Schering AG, Dept Expt Dermatol, D-13342 Berlin, Germany; Schering AG, Enabeling Technol Genom & Bioinformat, D-13342 Berlin, Germany; Humboldt Univ, Med Sch Charite, Inst Med Immunol, D-10098 Berlin, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: GENES AND IMMUNITY, (OCT 2001) Vol. 2, No. 6, pp. 329-334. Publisher: NATURE PUBLISHING GROUP, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND.
ISSN: 1466-4879.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 34

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The cytokine receptor family type 2 (CRF2) comprises receptors for important immunomediators like interferons and interleukin-10 (IL-10). We identified a novel member of this family which represents the first exclusively soluble receptor in this group and was therefore designated as CRF2-soluble 1 (CRF2-s1). The CRF2-s1 gene covers about 28 kb and is located on chromosome 6 in close proximity to the CRF2 members interferon (IFN)-gamma receptor 1 and IL-20 receptor 1. It comprises seven exons and generates two different mRNA splice **variants**, CRF2-s1-long and CRF2-s1-short. CRF2-s1-long and CRF2-s1-short encode proteins of 263 and 231 amino acids, respectively. A comparison of predicted protein structures led to the postulation that each receptor **variants** binds a different ligand. Quantitative analysis of human mRNA expression revealed a very restricted pattern for both splice forms. CRF2-s1 turned out to be the first member of this receptor family which was expressed neither in resting nor in stimulated leucocyte populations. CRF2-s1-long was only expressed in placenta, whereas CRF2-s1-short was additionally expressed in human mammary gland and, at a lower level, in skin, spleen, thymus and stomach. The preferential expression of CRF2-s1 in placenta suggests a role for this receptor in establishing and maintaining successful pregnancy.

L15 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:35928 CAPLUS
DOCUMENT NUMBER: 135:237339
TITLE: IL-TIF/**IL-22**: Genomic organization and mapping of the human and mouse genes
AUTHOR(S): Dumoutier, L.; Van Roost, E.; Ameye, G.; Michaux, L.; Renauld, J-C.
CORPORATE SOURCE: Brussels Branch, Ludwig Institute for Cancer Research, Brussels, B-1200, Belg.
SOURCE: Genes and Immunity (2000), 1(8), 488-494
CODEN: GEIMA2; ISSN: 1466-4879
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB IL-TIF is a new cytokine originally identified as a gene induced by IL-9 in murine T lymphocytes, and showing 22% amino acid identity with IL-10. Here, we report the sequence and organization of the mouse and human IL-TIF genes, which both consist of 6 exons spreading over approx. 6 Kb. The IL-TIF gene is a single copy gene in humans, and is located on chromosome 12q15, at 90 Kb from the IFN.gamma. gene, and at 27 Kb from the AK 155 gene, which codes for another IL-10-related cytokine. In the mouse, the IL-TIF gene is located on chromosome 10, also in the same region as the IFN.gamma. gene. Although it is a single copy gene in BALB/c and DBA/2 mice, the IL-TIF gene is duplicated in other strains such as C57Bl/6, FVB and 129. The two copies, which show 98% nucleotide identity in the coding region, were named IL-TIF.alpha. and IL-TIF.beta.. Beside single nucleotide variations, they differ by a 658 nucleotide deletion in IL-TIF.beta., including the first non-coding exon and 603 nucleotides from the promoter. A DNA fragment corresponding to this deletion was sufficient to confer IL-9-regulated expression of a luciferase reporter plasmid, suggesting that the IL-TIF.beta. gene is either differentially regulated, or not expressed at all.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s (interleukin-22 or il-22)
L16 47 FILE MEDLINE
L17 90 FILE CAPLUS
L18 60 FILE SCISEARCH
L19 27 FILE LIFESCI
L20 54 FILE BIOSIS
L21 49 FILE EMBASE

TOTAL FOR ALL FILES
L22 327 (INTERLEUKIN-22 OR IL-22)

=> s l22 and (crystal or x-ray or nmr or structure)
L23 10 FILE MEDLINE

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L24          18 FILE CAPLUS
L25          15 FILE SCISEARCH
L26           4 FILE LIFESCI
L27          33 FILE BIOSIS
L28          11 FILE EMBASE

TOTAL FOR ALL FILES
L29          91 L22 AND (CRYSTAL OR X-RAY OR NMR OR STRUCTURE)

=> s l29 not 2003-2004/py
L30           5 FILE MEDLINE
L31           7 FILE CAPLUS
L32           9 FILE SCISEARCH
L33           3 FILE LIFESCI
L34          19 FILE BIOSIS
L35           6 FILE EMBASE

TOTAL FOR ALL FILES
L36          49 L29 NOT 2003-2004/PY

=> dup rem l36
PROCESSING COMPLETED FOR L36
L37          24 DUP REM L36 (25 DUPLICATES REMOVED)

=> d ibib abs

L37  ANSWER 1 OF 24  BIOSIS  COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER:    2002:582423  BIOSIS
DOCUMENT NUMBER:     PREV200200582423
TITLE:               Interleukin-22 (IL-22
                     ) activates the JAK/STAT, ERK, JNK, and p38 MAP kinase
                     pathways in a rat hepatoma cell line. Pathways that are
                     shared with and distinct from IL-10.
AUTHOR(S):           Lejeune, Diane; Dumoutier, Laure; Constantinescu, Stefan;
                     Kruijer, Wiebe; Schuringa, Jan Jacob; Renauld,
                     Jean-Christophe [Reprint author]
CORPORATE SOURCE:    Ludwig Institute for Cancer Research, Ave. Hippocrate, 74,
                     B-1200, Brussels, Belgium
                     renauld@licr.ucl.ac.be
SOURCE:              Journal of Biological Chemistry, (September 13, 2002) Vol.
                     277, No. 37, pp. 33676-33682. print.
                     CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE:       Article
LANGUAGE:            English
ENTRY DATE:          Entered STN: 13 Nov 2002
                     Last Updated on STN: 30 Dec 2002
AB   IL (interleukin)-22 is an IL-10-related cytokine; its
     main biological activity known thus far is the induction of acute phase
     reactants in liver and pancreas.  IL-22 signals
     through a receptor that is composed of two chains from the class II
     cytokine receptor family: IL-22R (also called ZcytoR11/CRF2-9) and
     IL-10Rbeta (CRF2-4), which is also involved in IL-10 signaling.  In this
     report, we analyzed the signal transduction pathways activated in response
     to IL-22 in a rat hepatoma cell line, H4IIE.  We found
     that IL-22 induces activation of JAK1 and Tyk2 but not
     JAK2, as well as phosphorylation of STAT1, STAT3, and STAT5 on tyrosine
     residues, extending the similarities between IL-22 and
     IL-10.  However our results unraveled some differences between IL
     -22 and IL-10 signaling.  Using antibodies specific for the
     phosphorylated form of MEK1/2, ERK1/2, p90RSK, JNK, and p38 kinase, we
     showed that IL-22 activates the three major MAPK
     pathways.  IL-22 also induced serine phosphorylation
     of STAT3 on Ser727.  This effect, which is not shared with IL-10, was only
     marginally affected by MEK1/2 inhibitors, indicating that other pathways
     might be involved.  Finally, by overexpressing a STAT3 S727A mutant, we
     showed that serine phosphorylation is required to achieve maximum
     transactivation of a STAT responsive promoter upon IL-22
     stimulation.


=> d ibib abs 2-24
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L37 ANSWER 2 OF 24 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 1
ACCESSION NUMBER: 2002:592275 SCISEARCH
THE GENUINE ARTICLE: 571YP
TITLE: The conserved helix C region in the superfamily of interferon-gamma/interleukin-10-related cytokines corresponds to a high-affinity binding site for the HSP70 chaperone DnaK
AUTHOR: Vandenbroeck K (Reprint); Alloza I; Brehmer D; Billiau A; Proost P; McFerran N; Rudiger S; Walker B
CORPORATE SOURCE: Queens Univ Belfast, Sch Pharm, Cytokine Biol & Genet Programme, Mcclay Res Ctr Pharmaceut Sci, Biomol Sci Res Grp, 97 Lisburn Rd, Belfast BT9 7BL, Antrim, North Ireland (Reprint); Queens Univ Belfast, Sch Pharm, Cytokine Biol & Genet Programme, Mcclay Res Ctr Pharmaceut Sci, Biomol Sci Res Grp, Belfast BT9 7BL, Antrim, North Ireland; Queens Univ Belfast, Ctr Prot & Peptide Engn, Belfast BT9 7BL, Antrim, North Ireland; Univ Freiburg, Inst Biochem & Mol Biol, D-79104 Freiburg, Germany; Catholic Univ Louvain, Rega Inst Med Res, B-3000 Louvain, Belgium; Univ Cambridge, MRC, Ctr Prot Engn, Cambridge CB2 2QH, England
COUNTRY OF AUTHOR: North Ireland; Germany; Belgium; England
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (12 JUL 2002) Vol. 277, No. 28, pp. 25668-25676.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 59
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB HSP70 chaperones mediate protein folding by ATP-dependent interaction with short linear peptide segments that are exposed on unfolded proteins. The mode of action of the Escherichia coli homolog DnaK is representative of all HSP70 chaperones, including the endoplasmic reticulum variant BiP/GRP78. DnaK has been shown to be effective in assisting refolding of a wide variety of prokaryotic and eukaryotic proteins, including the alpha-helical homodimeric secretory cytokine interferon-gamma (IFN-gamma). We screened solid-phase peptide libraries from human and mouse IFN-gamma to identify DnaK-binding sites. Conserved DnaK-binding sites were identified in the N-terminal half of helix B and in the C-terminal half of helix C, both of which are located at the IFN-gamma dimer interface. Soluble peptides derived from helices B and C bound DnaK with high affinity in competition assays. No DnalK-binding sites were found in the loops connecting the alpha-helices. The helix C DnaK-binding site appears to be conserved in most members of the superfamily of interleukin (IL)-10-related cytokines that comprises, apart from IL-10 and IFN-gamma, a series of recently discovered small secretory proteins, including IL-19, IL-20, **IL-22**/IL-TIF, IL-24/MDA-7 (melanoma differentiation-associated gene), IL-26/AK155, and a number of viral IL-10 homologs. These cytokines belong to a relatively small group of homodimeric proteins with highly interdigitated interfaces that exhibit the strongly hydrophobic character of the interior core of a single-chain folded domain. We propose that binding of DnaK to helix C in the superfamily of IL-10-related cytokines may constitute the hallmark of a novel conserved regulatory mechanism in which HSP70-like chaperones assist in the formation of a hydrophobic dimeric "folding" interface.

L37 ANSWER 3 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:359022 BIOSIS
DOCUMENT NUMBER: PREV200200359022
TITLE: Cutting edge: Immune cells as sources and targets of the IL-10 family members?.
AUTHOR(S): Wolk, Kerstin; Kunz, Stefanie; Asadullah, Khusru; Sabat, Robert [Reprint author]
CORPORATE SOURCE: Department of Experimental Dermatology, Schering AG, Muellerstrasse 178, D-13342, Berlin, Germany
robert.sabat@schering.de
SOURCE: Journal of Immunology, (June 1, 2002) Vol. 168, No. 11, pp. 5397-5402. print.
CODEN: JOIMA3. ISSN: 0022-1767.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jun 2002
Last Updated on STN: 26 Jun 2002

AB This study investigated the expression of five novel human IL-10-related molecules and their receptors in blood mononuclear cells. IL-19 and IL-20 were found to be preferentially expressed in monocytes. **IL-22** and IL-26 (AK155) expression was exclusively detected in T cells, especially upon type 1 polarization, and in NK cells. IL-24 (melanoma differentiation-associated gene 7) expression was restricted to monocytes and T cells. Detection of these molecules in lymphocytes was predominantly linked to cellular activation. Regarding T cells, IL-26 was primarily produced by memory cells, and its expression was independent on costimulation. In contrast to the high expression of receptors for IL-10 homologs in different tissues and cell lines, monocytes and NK, B, and T cells showed clear expression only of IL-10R1, IL-10R2, and IL-20R2. In these cells, IL-20R2 might be part of a still-unknown receptor complex. Therefore, immune cells may represent a major source but a minor target of the novel IL-10 family members.

L37 ANSWER 4 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:590852 BIOSIS
DOCUMENT NUMBER: PREV200200590852
TITLE: IL-19 induces production of IL-6 and TNF-alpha and results in cell apoptosis through TNF-alpha.
AUTHOR(S): Liao, Yuan-Chun; Liang, Wei-Guang; Chen, Feng-Wei; Hsu, Ju-Hui; Yang, Jiann-Jou; Chang, Ming-Shi [Reprint author]
CORPORATE SOURCE: College of Medicine, Graduate Institute of Biochemistry, National Cheng Kung University, Tainan, 70, Taiwan
mschang@mail.ncku.edu.tw
SOURCE: Journal of Immunology, (October 15, 2002) Vol. 169, No. 8, pp. 4288-4297. print.
CODEN: JOIMA3. ISSN: 0022-1767.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2002
Last Updated on STN: 13 Nov 2002

AB IL-10 is an immunosuppressive cytokine in the immune system. It was in clinical trail as an anti-inflammatory therapy for inflammatory bowel disease and various autoimmune diseases such as psoriasis, rheumatoid arthritis, and multiple sclerosis. IL-19 belongs to the IL-10 family, which includes IL-10, IL-19, IL-20, **IL-22**, melanoma differentiation-associated gene (MDA-7, IL-24), and AK155 (IL-26). Despite a partial homology in their amino acid sequences, they are dissimilar in their biologic functions. Little is known about the biologic function and gene regulation of IL-19. To understand the gene regulation of human IL-19, we identified a human IL-19 genomic clone and analyzed its promoter region. Five fusion genes containing different regions upstream of exon 1 linked to a luciferase reporter gene were expressed in the canine kidney epithelial-like Madin-Darby canine kidney cells. A fusion gene containing 394 bp showed luciferase activity 7- to 8-fold higher than the negative control of the promoterless fusion gene. We also isolated a full-length mouse cDNA clone. Mouse IL-19 shared 71% amino acid identity with human IL-19. Treatment of monocytes with mouse IL-19 induced the production of IL-6 and TNF-alpha. It also induced mouse monocyte apoptosis and the production of reactive oxygen species. Taken together, our results indicate that mouse IL-19 may play some important roles in inflammatory responses because it up-regulates IL-6 and TNF-alpha and induces apoptosis.

L37 ANSWER 5 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:34926 BIOSIS
DOCUMENT NUMBER: PREV200300034926
TITLE: **IL-22**, in contrast to IL-10, does not induce Ig production, due to absence of a functional **IL-22** receptor on activated human B cells.
AUTHOR(S): Lecart, Sandrine; Morel, Frank; Noraz, Nelly; Pene, Jerome; Garcia, Martine; Boniface, Katia; Lecron, Jean-Claude; Yssel, Hans [Reprint Author]
CORPORATE SOURCE: INSERM U454, CHU Arnaud de Villeneuve, 371, Avenue Doyen

Gaston Giraud, 34295, Montpellier Cedex 5, France
yssel@montp.inserm.fr
SOURCE: International Immunology, (November 2002) Vol. 14, No. 11, pp. 1351-1356. print.
ISSN: 0953-8178.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jan 2003
Last Updated on STN: 8 Jan 2003
AB **IL-22** is an IL-10 homologue that binds to and signals via the class II cytokine receptor (R) heterodimer IL-22RA1/CFR2-4 (IL-10R2), the latter chain being part of the IL-10R complex. Here, we report that, despite its structural similarity with IL-10, as well as its use of the common IL-10R2 chain, **IL-22**, in contrast to IL-10, is unable to induce Ig production by activated human B cells. Whereas culture of anti-CD40 mAb-stimulated splenic or tonsillar B cells in the presence of rIL-10 resulted in the production of IgG, IgG1, IgG3 and IgA, rIL-22, at concentrations ranging from 4 to 100 ng/ml, did not induce the production of any of these isotypes. Moreover, unlike rIL-10 which enhanced rIL-4-induced IgG4 and IgE production, rIL-22 was ineffective. Although activated B cells expressed transcripts for a soluble **IL-22**-binding protein (IL-22RA2), no mRNA for a transmembrane IL-22R (IL-22RA1) could be detected. The latter result was confirmed by the demonstration that rIL-22 failed to induce activation of STAT-3 and -5 in resting or activated B cells. Together, these data show that **IL-22**, in contrast to its homologue IL-10, is not involved in the immunological activity of B cells, which is due to the absence of a functional IL-22R at the surface of these cells.

L37 ANSWER 6 OF 24 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003008761 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12513909
TITLE: Comparison of **interleukin-22** and interleukin-10 soluble receptor complexes.
AUTHOR: Logsdon Naomi J; Jones Brandi C; Josephson Kristopher; Cook Jennifer; Walter Mark R
CORPORATE SOURCE: Department of Microbiology and Center for Biophysical Sciences and Engineering, University of Alabama at Birmingham, AL 35294, USA.
SOURCE: Journal of interferon & cytokine research : official journal of the International Society for Interferon and Cytokine Research, (2002 Nov) 22 (11) 1099-112.
Journal code: 9507088. ISSN: 1079-9907.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030108
Last Updated on STN: 20030718
Entered Medline: 20030717
AB **Interleukin-22** (**IL-22**) is a cellular homolog of IL-10 that stimulates the production of acute-phase reactants. **IL-22** and IL-10 require different ligand-specific receptor chains (IL-22R and IL-10R1) but share a second receptor chain (IL-10R2) to initiate cellular responses. The quaternary **structures** and the ability of **IL-22** and IL-10 to engage soluble (s) IL-10R1, IL-22R, IL-10R2 receptor chains were analyzed using size exclusion chromatography and surface plasmon resonance techniques. In contrast to IL-10, which is a homodimer, **IL-22** is a monomer in solution that forms a 1:1 interaction with sIL-22R. Kinetic binding data reveal sIL-22R and sIL-10R1 exhibit specific nanomolar binding constants for **IL-22** (k(on)/k(off) = 14.9 nM) and a monomeric isomer of IL-10 (IL-10M1) (k(on)/k(off) = 0.7 nM), respectively. In contrast, IL-10R2 exhibits essentially no affinity for **IL-22** (K(eq) approximately 1 mM) or IL-10M1 (K(eq) approximately 2 mM) alone but displays a substantial increase in affinity for the IL-10/sIL-10R1 (K(eq) approximately 350 microM) and **IL-22**/sIL-22R (K(eq) approximately 45 microM) complexes. Three-dimensional models of **IL-22** and IL-10 receptor complexes suggest two receptor

residues (Gly-44 and Arg-96) are largely responsible for the marked differences in ligand affinity observed for sIL-10R1 and sIL-22R vs. sIL-10R2.

L37 ANSWER 7 OF 24 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002422601 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12176383
TITLE: **Crystal structure** of recombinant human **interleukin-22.**
AUTHOR: Nagem Ronaldo Alves Pinto; Colau Didier; Dumoutier Laure; Renauld Jean-Christophe; Ogata Craig; Polikarpov Igor
CORPORATE SOURCE: Laboratorio Nacional de Luz Sincrotron, Sao Paulo, Brazil.
SOURCE: Structure (Cambridge, Mass. : 2001), (2002 Aug) 10 (8) 1051-62.
Journal code: 101087697. ISSN: 0969-2126.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1M4R
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20020815
Last Updated on STN: 20030305
Entered Medline: 20030304
AB **Interleukin-22** (IL-10-related T cell-derived inducible factor/IL-TIF/**IL-22**) is a novel cytokine belonging to the IL-10 family. Recombinant human **IL-22** (hIL-22) was found to activate the signal transducers and activators of transcription factors 1 and 3 as well as acute phase reactants in several hepatoma cell lines, suggesting its involvement in the inflammatory response. The crystallographic **structure** of recombinant hIL-22 has been solved at 2.0 A resolution using the SIRAS method. Contrary to IL-10, the hIL-22 dimer does not present an interpenetration of the secondary-**structure** elements belonging to the two distinct polypeptide chains but results from interface interactions between monomers. Structural differences between these two cytokines, revealed by the crystallographic studies, clearly indicate that, while a homodimer of IL-10 is required for signaling, hIL-22 most probably interacts with its receptor as a monomer.

L37 ANSWER 8 OF 24 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2002148595 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11856845
TITLE: Crystallization and synchrotron **X-ray** diffraction studies of human **interleukin-22.**
AUTHOR: Nagem R A P; Lucchesi K W; Colau D; Dumoutier L; Renauld J-C; Polikarpov I
CORPORATE SOURCE: Laboratorio Nacional de Luz Sincrotron, Caixa Postal 6192, CEP 13083-970, Campinas, SP, Brazil.
SOURCE: Acta crystallographica. Section D, Biological crystallography, (2002 Mar) 58 (Pt 3) 529-30.
Journal code: 9305878. ISSN: 0907-4449.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020308
Last Updated on STN: 20020619
Entered Medline: 20020618
AB Human **interleukin-22**, a novel member of the cytokine family, has been crystallized in hanging drops using the vapour-diffusion technique. Preliminary **X-ray** diffraction experiments using synchrotron radiation reveal that the protein crystallizes in space group P2(1)2(1)2(1), with unit-cell parameters a = 55.44, b = 61.62, c = 73.43 A, and diffracts beyond 2.00 A resolution.

L37 ANSWER 9 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:177810 BIOSIS
DOCUMENT NUMBER: PREV200300177810

TITLE: Linkage disequilibrium analysis of chromosome 12q14-15 in multiple sclerosis: Delineation of a 118-kb interval around interferon-gamma (IFNG) that is involved in male versus female differential susceptibility.

AUTHOR(S): Goris, A.; Heggarty, S.; Marrosu, M. G.; Graham, C.; Billiau, A.; Vandenbroeck, K. [Reprint Author]

CORPORATE SOURCE: Cytokine Biology and Genetics Programme, School of Pharmacy, Queen's University of Belfast, 97 Lisburn Road, Belfast, BT9 7BL, UK
k.vandenbroeck@qub.ac.uk

SOURCE: Genes and Immunity, (December 2002) Vol. 3, No. 8, pp. 470-476. print.
ISSN: 1466-4879 (ISSN print).

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Apr 2003
Last Updated on STN: 9 Apr 2003

AB We have recently reported the association of a polymorphic intronic CA-repeat in the interferon-gamma gene (IFNG) with gender bias in susceptibility to multiple sclerosis (MS) in a Sardinian population. This association could refer to a functional polymorphism within IFNG or could be due to linkage disequilibrium between the IFNG marker and a neighbouring susceptibility locus. Within the average reach of linkage disequilibrium, various other candidate genes are located. Among these the most striking ones are the genes coding for the cytokines **interleukin-22** (**IL-22**) and interleukin-26 (IL-26) that constitute together with IFNG a cytokine cluster on chromosome 12q14. To determine more precisely the location of this gender-associated susceptibility locus, we have now performed a more extensive linkage disequilibrium screen of this region using nine additional microsatellite markers. This locus appeared to be confined to a 118-kb interval that is bordered by the markers D12S313 and D12S2511, in which IFNG itself remains the main candidate gene. Haplotype analysis confirmed that this MS-associated locus protects males from developing MS according to a recessive or allele-dosage model. Our results indicate that the well-documented gender differences in susceptibility to MS are at least partially caused by genetic factors in the region surrounding IFNG.

L37 ANSWER 10 OF 24 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2002:854841 SCISEARCH
THE GENUINE ARTICLE: 604KU

TITLE: **Structure** of interleukin-10/interleukin-10R1 complex - A paradigm for class 2 cytokine activation

AUTHOR: Walter M R (Reprint)
CORPORATE SOURCE: Univ Alabama, Dept Microbiol, Birmingham, AL 35294 USA (Reprint)
COUNTRY OF AUTHOR: USA

SOURCE: IMMUNOLOGIC RESEARCH, (OCT 2002) Vol. 26, No. 1-3, pp. 303-308.
Publisher: HUMANA PRESS INC, 999 RIVERVIEW DRIVE SUITE 208, TOTOWA, NJ 07512 USA.
ISSN: 0257-277X.

DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 10

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The class 11 alpha-helical cytokine family consists of eleven members including the interferons, interleukin-10 (IL-10) and several newly discovered IL-10 homologs. The molecules display a vast array of biologic activities including the ability to induce an antiviral state, modulate inflammatory responses, and inhibit cell growth. Biologic activity is dependent on cytokine-dependent aggregation of two different cell-surface receptors. The detailed protein-protein interactions that initiate these biologic responses are amenable to study using **X-ray** crystallographic methods. In this article, I summarize my laboratory's contributions to understanding these recognition processes using IL-10 as the prototypic class 11 cytokine.

L37 ANSWER 11 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5

ACCESSION NUMBER: 2002:487454 BIOSIS

DOCUMENT NUMBER: PREV200200487454
TITLE: The family of IL-10-related cytokines and their receptors: Related, but to what extent?.
AUTHOR(S): Kotenko, Sergei V. [Reprint author]
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, New Jersey Medical School, University of Medicine and Dentistry, 185 South Orange Avenue, MSB E-631, Newark, NJ, 07103, USA
kotenkse@umdnj.edu
SOURCE: Cytokine and Growth Factor Reviews, (June, 2002) Vol. 13, No. 3, pp. 223-240. print.
ISSN: 1359-6101.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Sep 2002
Last Updated on STN: 18 Sep 2002

L37 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2002:499938 CAPLUS
DOCUMENT NUMBER: 138:13222
TITLE: Novel interleukins: IL-19, IL-20, IL-21, **IL-22**, IL-23
AUTHOR(S): Kasakura, Shinpei
CORPORATE SOURCE: Department of Medicine, Kobe City General Hospital, Japan
SOURCE: Biotherapy (Tokyo, Japan) (2002), 16(3), 193-203
CODEN: BITPE9; ISSN: 0914-2223
PUBLISHER: Gan to Kagaku Ryohosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. Today, more than 50 cytokines have been identified and more cytokines and receptor mols. will continue to be discovered at a good pace through searches for sequence homol. in sequence databases. Recently, a family of cytokines with limited homol. to IL-10 has been identified. They include IL-10, IL-20 and **IL-22**. The genes of IL-10, IL-19 and IL-20 are mapped to human chromosome 1 q 31-32, whereas **IL-22** is located on chromosome 12 q 15, near the IFN-.gamma. gene. These IL-10-related cytokines share receptor subunits of the class II cytokine receptor family, also known as the interferon receptor family. The IL-10R.beta. subunit is involved in both IL-10 and **IL-22** signaling. The IL-20R.beta. subunit can assoc. with IL-20R.alpha., leading to a functional receptor for IL-20. IL-20 and **IL-22** induce, resp., keratinocyte proliferation and acute phase reactant prodn. by liver cells. The ability of **IL-22** to suppress IL-4 prodn. from Th2 cells may have therapeutic potential in the treatment of allergic diseases. For IL-19, no activity or receptor complex has been described thus far. A new class I cytokine receptor, IL-21R, was identified through searches for sequence homol. in expressed sequence tag (EST) contg. a predicted signal peptide and a predicted amphipathic helix. IL-21R is selectively expressed in lymphoid tissues. The ligand IL-21 was identified and cloned by the use of a proliferation assay based on BaF3 cells expressing IL-21R. IL-21 is most closely related to IL-2 and IL-15. IL-21 has a role in the proliferation and maturation of NK cells from bone marrow, and in the proliferation of both T and B cells. A novel cytokine, p19 was identified by searching sequence databases with a computationally derived profile of IL-6 superfamily **structures**. P19 shows no biol. activity by itself. It combines with the p40 subunit of IL-12 to form a novel, biol. active cytokine which is termed IL-23. The IL-12R .beta.1 subunit may be involved in both IL-12 and IL-23 signaling. Similar to IL-12, human IL-23 stimulates IFN-.gamma. prodn. and proliferation in PHA blast T cells, as well as in memory T cells.

L37 ANSWER 13 OF 24 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002195282 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11929132
TITLE: The interleukin-10 family of cytokines.
AUTHOR: Fickenscher Helmut; Hor Simon; Kupers Heide; Knappe Andrea; Wittmann Sabine; Sticht Heinrich
CORPORATE SOURCE: Hygiene-Institut, Abteilung Virologie, Ruprecht-Karls-

Universitat Heidelberg, Germany.
SOURCE: Trends in immunology, (2002 Feb) 23 (2) 89-96.
Journal code: 100966032. ISSN: 1471-4906.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020404
Last Updated on STN: 20020528
Entered Medline: 20020523

AB A family of interleukin-10 (IL-10)-related cytokines has emerged, comprising a series of herpesviral and poxviral members and several cellular sequence paralogs, including IL-19, IL-20, **IL-22** [IL-10-related T-cell-derived inducible factor (IL-TIF)], IL-24 [melanoma differentiation-associated antigen 7 (MDA-7)] and IL-26 (AK155). Although the predicted helical **structure** of these homodimeric molecules is conserved, certain receptor-binding residues are variable and define the interaction with specific heterodimers of different type-2 cytokine receptors. This leads, through the activation of signal transducer and activator of transcription (STAT) factors, to diverse biological effects. For example, whereas IL-10 is a well-studied pleiotropic immunosuppressive and immunostimulatory cytokine, **IL-22**/IL-TIF mediates acute-phase response signals in hepatocytes and IL-20 induces the hyperproliferation of keratinocytes, which has been proposed as a pathogenic mechanism of psoriasis.

L37 ANSWER 14 OF 24 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2002219324 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11956016
TITLE: Viral and cellular interleukin-10 (IL-10)-related cytokines: from **structures** to functions.
AUTHOR: Dumoutier Laure; Renauld Jean-Christophe
CORPORATE SOURCE: Ludwig Institute for Cancer Research, UCL 74 59, Avenue Hippocrate, 74, B-1200 Brussels, Belgium.
SOURCE: European cytokine network, (2002 Jan-Mar) 13 (1) 5-15.
Ref: 97
Journal code: 9100879. ISSN: 1148-5493.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020417
Last Updated on STN: 20020927
Entered Medline: 20020926

AB The anti-inflammatory and immunosuppressive activities of IL-10 have been extensively studied during the last 10 years. More recently a series of new cytokines, structurally related to IL-10, were described. This family includes mda-7, IL-19, IL-20, IL-TIF/**IL-22**, and AK155.
Most of the biological functions of these cytokines remain to be unraveled but new data are coming out steadily. Although none of these "IL-10 homologs" mimics IL-10 activities, they are likely to be involved in inflammatory processes as well. mda-7, IL-19 and IL-20 form a subfamily within IL-10 homologs, based on conserved amino acid sequences, and on the use of shared receptor complexes. Functional studies have stressed the potential suppressing activity of mda-7 on tumor growth. As for IL-20, its overexpression in transgenic mice led to skin abnormalities, reminiscent of psoriatic lesions in humans. IL-TIF/**IL-22** is a Th1 cytokine, and was shown to upregulate the acute phase reactant production by liver cells. Finally, for AK155, originally described as a gene induced upon T cell transformation by Herpes-virus saimiri, functional data are still lacking to determine its biological activities.

L37 ANSWER 15 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:51940 BIOSIS
DOCUMENT NUMBER: PREV200300051940
TITLE: Immune cells as sources and targets of the interleukin-10

family members?.
AUTHOR(S): Wolk, K.; Kunz, S.; Asadullah, K.; Sabat, R.
SOURCE: Journal of Interferon and Cytokine Research, (2002) Vol. 22, No. Supplement 1, pp. S-97-S-98. print.
Meeting Info.: Joint Meeting of the International Society for Interferon and Cytokine Research, the International Cytokine Society, the Society for Leukocyte Biology, and the European Cytokine Society on Cytokines and Interferons. Turin, Italy. October 06-10, 2002. International Society for Interferon and Cytokine Research.
ISSN: 1079-9907 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jan 2003
Last Updated on STN: 22 Jan 2003

L37 ANSWER 16 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:65091 BIOSIS
DOCUMENT NUMBER: PREV200300065091
TITLE: Overlapping ligand specificities but divergent function in the IL-20 subfamily.
AUTHOR(S): Parrish-Novak, J. [Reprint Author]; Xu, W. [Reprint Author]; Brender, T. [Reprint Author]; Yao, L. [Reprint Author]; Jones, C. [Reprint Author]; West, J. [Reprint Author]; Brandt, C. [Reprint Author]; Jelinek, L. [Reprint Author]; Madden, K. [Reprint Author]; McKernan, P. A. [Reprint Author]; Foster, D. C. [Reprint Author]; Jaspers, S. [Reprint Author]; Chandrasekher, Y. A. [Reprint Author]
CORPORATE SOURCE: ZymoGenetics, Inc., 1201 Eastlake Avenue East, Seattle, WA, 98102, USA
SOURCE: Journal of Interferon and Cytokine Research, (2002) Vol. 22, No. Supplement 1, pp. S-46. print.
Meeting Info.: Joint Meeting of the International Society for Interferon and Cytokine Research, the International Cytokine Society, the Society for Leukocyte Biology, and the European Cytokine Society on Cytokines and Interferons. Turin, Italy. October 06-10, 2002. International Society for Interferon and Cytokine Research.
ISSN: 1079-9907 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003

L37 ANSWER 17 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:427311 BIOSIS
DOCUMENT NUMBER: PREV200100427311
TITLE: A soluble class II cytokine receptor, IL-22RA2, is a naturally occurring **IL-22** antagonist.
AUTHOR(S): Xu, Wenfeng; Presnell, Scott R.; Parrish-Novak, Julia; Kindsvogel, Wayne; Jaspers, Steve; Chen, Zhi; Dillon, Stacey R.; Gao, Zeren; Gilbert, Teresa; Madden, Karen; Schlutsmeyer, Stacy; Yao, Lena; Whitmore, Theodore E.; Chandrasekher, Yasmin; Grant, Francis J.; Maurer, Mark; Jelinek, Laura; Storey, Harold; Brender, Ty; Hammond, Angie; Topouzis, Stavros; Clegg, Christopher H.; Foster, Donald C. [Reprint author]
CORPORATE SOURCE: ZymoGenetics Inc., 1201 Eastlake Avenue East, Seattle, WA, 98102, USA
DOFO@zgi.com
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (August 14, 2001) Vol. 98, No. 17, pp. 9511-9516. print.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Sep 2001
Last Updated on STN: 22 Feb 2002
AB **IL-22** is an IL-10 homologue that binds to and signals

through the class II cytokine receptor heterodimer IL-22RA1/CRF2-4. **IL-22** is produced by T cells and induces the production of acute-phase reactants in vitro and in vivo, suggesting its involvement in inflammation. Here we report the identification of a class II cytokine receptor designated IL-22RA2 (**IL-22** receptor-alpha 2) that appears to be a naturally expressed soluble receptor. IL-22RA2 shares amino acid sequence homology with IL-22RA1 (also known as IL-22R, zcytor11, and CRF2-9) and is physically adjacent to IL-20R alpha and IFN-gammaR1 on chromosome 6q23.3-24.2. We demonstrate that IL-22RA2 binds specifically to **IL-22** and neutralizes **IL-22**-induced proliferation of BaF3 cells expressing **IL-22** receptor subunits. IL-22RA2 mRNA is highly expressed in placenta and spleen by Northern blotting. PCR analysis using RNA from various tissues and cell lines showed that IL-22RA2 was expressed in a range of tissues, including those in the digestive, female reproductive, and immune systems. In situ hybridization revealed the dominant cell types expressing IL-22RA2 were mononuclear cells and epithelium. Because **IL-22** induces the expression of acute phase reactants, IL-22RA2 may play an important role as an **IL-22** antagonist in the regulation of inflammatory responses.

L37 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:447464 CAPLUS
DOCUMENT NUMBER: 135:194244
TITLE: Identification, cloning, and characterization of a novel soluble receptor that binds **IL-22** and neutralizes its activity
AUTHOR(S): Kotenko, Sergei V.; Izotova, Lara S.; Mirochnitchenko, Olga V.; Esterova, Elena; Dickensheets, Harold; Donnelly, Raymond P.; Pestka, Sidney
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Robert Wood Johnson Medical School, University of Medicine and Dentistry, Piscataway, NJ, 08854, USA
SOURCE: Journal of Immunology (2001), 166(12), 7096-7103
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB With the use of a partial sequence of the human genome, the authors identified a gene encoding a novel sol. receptor belonging to the class II cytokine receptor family. This gene is positioned on chromosome 6 in the vicinity of the IFNGR1 gene in a head-to-tail orientation. The gene consists of six exons and encodes a 231-aa protein with a 21-aa leader sequence. The secreted mature protein demonstrates 34% amino acid identity to the extracellular domain of the IL-22R1 chain. Crosslinking expts. demonstrate that the protein binds **IL-22** and prevents binding of **IL-22** to the functional cell surface IL-22R complex, which consists of two subunits, the IL-22R1 and the IL-10R2c chains. Moreover, this sol. receptor, designated **IL-22**-binding protein (BP), is capable of neutralizing **IL-22** activity. In the presence of the IL-22BP, **IL-22** is unable to induce Stat activation in **IL-22**-responsive human lung carcinoma A549 cells. IL-22BP also blocked induction of the suppressors of cytokine signaling-3 (SOCS-3) gene expression by **IL-22** in HepG2 cells. To further evaluate IL-22BP action, the authors used hamster cells expressing a modified IL-22R complex consisting of the intact IL-10R2c and the chimeric IL-22R1/.gamma.R1 receptor in which the IL-22R1 intracellular domain was replaced with the IFN-.gamma.R1 intracellular domain. In these cells, **IL-22** activates biol. activities specific for IFN-.gamma., such as up-regulation of MHC class I Ag expression. The addn. of IL-22BP neutralizes the ability of **IL-22** to induce Stat activation and MHC class I Ag expression in these cells. Thus, the sol. receptor designated IL-22BP inhibits **IL-22** activity by binding **IL-22** and blocking its interaction with the cell surface IL-22R complex.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 19 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:150013 BIOSIS

DOCUMENT NUMBER: PREV200200150013
TITLE: Acinar cells of the pancreas are a target of **interleukin-22**.
AUTHOR(S): Aggarwal, Sudeepta; Xie, Ming-Hong; Maruoka, Miko; Foster, Jessica; Gurney, Austin L. [Reprint author]
CORPORATE SOURCE: Department of Molecular Biology, Genentech, Inc., 1 DNA Way, South San Francisco, CA, 94080, USA nico@gene.com
SOURCE: Journal of Interferon and Cytokine Research, (December, 2001) Vol. 21, No. 12, pp. 1047-1053. print. ISSN: 1079-9907.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2002
Last Updated on STN: 26 Feb 2002

AB **Interleukin-22** (**IL-22**) (also reported as IL-10-related T cell-derived inducible factor, IL-TIF) is a recently identified cytokine found to signal through a receptor comprising the class II cytokine receptor family members IL-10Rbeta/CRF2-4 and IL-22R. Previous work has established that IL-10Rbeta, also a component of the IL-10R complex, exhibits a broad distribution of mRNA expression. Here, we observe that IL-22R exhibits a restricted expression pattern, with highest levels of mRNA expression in pancreas and detectable expression in multiple other tissues, particularly liver, small intestine, colon, and kidney. We find that isolated primary pancreatic acinar cells and the acinar cell line 266-6 respond to **IL-22** with activation of Stat3 and changes in gene transcription. **IL-22** mediates robust induction of mRNA for pancreatitis-associated protein (PAP1)/Reg2 and osteopontin (OPN). PAP1 is a secreted protein related to the Reg family of trophic factors and was initially characterized as a protein elevated in pancreatitis. In vivo injection of **IL-22** resulted in rapid induction of PAP1 in pancreas, a response not observed in mice deficient in IL-10Rbeta. These results support the conclusion that IL-10Rbeta is a required common component of both the IL-10 and **IL-22** receptors and suggest that **IL-22** may play a role in the immune response in pancreas.

L37 ANSWER 20 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:418733 BIOSIS
DOCUMENT NUMBER: PREV200200418733
TITLE: Novel cytokine **IL-22** administrated by adenovirus vector or as recombinant purified protein induces acute-phase responses and renal tubular basophilia in female C57BL/6 mice.
AUTHOR(S): Lambert, A. [Reprint author]; Goad, B.; Pittman, D.; Clark, E.; Block, L.; Wong, T.; Erickson, J.; Hayes, L.; Sheilds, K.; Deng, B.; Spaulding, V.; Annis, B.; Zollner, R.; Wang, I.; Kobayashi, M.; Thibodeaux, D.; Leonard, J.; Jacobs, K.; Fouser, L.
CORPORATE SOURCE: Andover, USA
SOURCE: Toxicologic Pathology, (November-December, 2001) Vol. 29, No. 6, pp. 712. print.
Meeting Info.: Sixteenth Aspen Cancer Conference on Mechanisms of Toxicity, Carcinogenesis, Cancer Prevention, and Cancer Therapy. Aspen, Colorado, USA. July 15-18, 2001.
CODEN: TOPADD. ISSN: 0192-6233.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Aug 2002
Last Updated on STN: 7 Aug 2002

L37 ANSWER 21 OF 24 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:806138 SCISEARCH
THE GENUINE ARTICLE: 479FW
TITLE: A novel, soluble homologue of the human IL-10 receptor with preferential expression in placenta
AUTHOR: Gruenberg B H; Schoenemeyer A; Weiss B; Toschi L; Kunz S; Wolk K; Asadullah K; Sabat R (Reprint)
CORPORATE SOURCE: Schering AG, Dept Expt Dermatol, Muellerstr 178, D-13342

Berlin, Germany (Reprint); Schering AG, Dept Expt Dermatol, D-13342 Berlin, Germany; Schering AG, Enabeling Technol Genom & Bioinformat, D-13342 Berlin, Germany; Humboldt Univ, Med Sch Charite, Inst Med Immunol, D-10098 Berlin, Germany

COUNTRY OF AUTHOR: Germany

SOURCE: GENES AND IMMUNITY, (OCT 2001) Vol. 2, No. 6, pp. 329-334. Publisher: NATURE PUBLISHING GROUP, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND. ISSN: 1466-4879.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 34

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The cytokine receptor family type 2 (CRF2) comprises receptors for important immunomediators like interferons and interleukin-10 (IL-10). We identified a novel member of this family which represents the first exclusively soluble receptor in this group and was therefore designated as CRF2-soluble 1 (CRF2-s1). The CRF2-s1 gene covers about 28 kb and is located on chromosome 6 in close proximity to the CRF2 members interferon (IFN)-gamma receptor 1 and IL-20 receptor 1. It comprises seven exons and generates two different mRNA splice variants, CRF2-s1-long and CRF2-s1-short. CRF2-s1-long and CRF2-s1-short encode proteins of 263 and 231 amino acids, respectively. A comparison of predicted protein **structures** led to the postulation that each receptor variants binds a different ligand. Quantitative analysis of human mRNA expression revealed a very restricted pattern for both splice forms. CRF2-s1 turned out to be the first member of this receptor family which was expressed neither in resting nor in stimulated leucocyte populations. CRF2-s1-long was only expressed in placenta, whereas CRF2-s1-short was additionally expressed in human mammary gland and, at a lower level, in skin, spleen, thymus and stomach. The preferential expression of CRF2-s1 in placenta suggests a role for this receptor in establishing and maintaining successful pregnancy.

L37 ANSWER 22 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:418139 BIOSIS

DOCUMENT NUMBER: PREV200200418139

TITLE: **IL-22** is a tightly regulated IL-10-like molecule that induces an acute-phase response and renal tubular basophilia.

AUTHOR(S): Fouser, Lynette A. [Reprint author]; Lambert, Andre-Jean [Reprint author]; Clark, Edward [Reprint author]; Deng, Bijia [Reprint author]; Tan, Xiang-Yang [Reprint author]; Spaulding, Vikki [Reprint author]; Wang, I-Ming [Reprint author]; Kobayashi, Michiko [Reprint author]; Whitters, Matthew [Reprint author]; Thibodeaux, Deborah [Reprint author]; Leonard, John [Reprint author]; Ling, Vincent [Reprint author]; Wu, Paul [Reprint author]; Annis, Bethany [Reprint author]; Lu, Zhijian [Reprint author]; Zollner, Richard [Reprint author]; Jacobs, Kenneth [Reprint author]; Goad, Beth [Reprint author]; Pittman, Debra [Reprint author]

CORPORATE SOURCE: Genetics Institute at WA-R, Cambridge, MA, 02140, USA

SOURCE: Journal of Leukocyte Biology Supplement, (2001) No. 2001, pp. 26. print.
Meeting Info.: Joint Meeting of the Society for Leukocyte Biology and the International Cytokine Society: The Cytokine Odyssey 2001. Maui, HI, USA. November 08-11, 2001. Society for Leukocyte Biology; International Cytokine Society.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 7 Aug 2002
Last Updated on STN: 7 Aug 2002

L37 ANSWER 23 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2000:513936 BIOSIS

DOCUMENT NUMBER: PREV200000513936

TITLE: Interleukin (**IL**)-**22**, a novel human

cytokine that signals through the interferon receptor-related proteins CRF2-4 and IL-22R.

AUTHOR(S): Xie, Ming-Hong; Aggarwal, Sudeepta; Ho, Wei-Hsien; Foster, Jessica; Zhang, Zemin; Stinson, Jeremy; Wood, William I.; Goddard, Audrey D.; Gurney, Austin L. [Reprint author]

CORPORATE SOURCE: Department of Molecular Biology, Genentech, Inc., South San Francisco, CA, 94080, USA

SOURCE: Journal of Biological Chemistry, (October 6, 2000) Vol. 275, No. 40, pp. 31335-31339. print.
CODEN: JBCHA3. ISSN: 0021-9258.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Nov 2000
Last Updated on STN: 11 Jan 2002

AB We report the identification of a novel human cytokine, distantly related to interleukin (IL)-10, which we term **IL-22**. **IL-22** is produced by activated T cells. **IL-22** is a ligand for CRF2-4, a member of the class II cytokine receptor family. No high affinity ligand has yet been reported for this receptor, although it has been reported to serve as a second component in IL-10 signaling. A new member of the interferon receptor family, which we term IL-22R, functions as a second component together with CRF2-4 to enable **IL-22** signaling. **IL-22** does not bind the IL-10R. Cell lines were identified that respond to **IL-22** by activation of STATs 1, 3, and 5, but were unresponsive to IL-10. In contrast to IL-10, **IL-22** does not inhibit the production of proinflammatory cytokines by monocytes in response to LPS nor does it impact IL-10 function on monocytes, but it has modest inhibitory effects on IL-4 production from Th2 T cells.

L37 ANSWER 24 OF 24 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 1998:781760 SCISEARCH

THE GENUINE ARTICLE: 125ZF

TITLE: Effect of SiGe thickness on crystallisation and electrical properties of sputtered silicon film in Si/SiGe/insulator **structure**

AUTHOR: Jelenkovic E V (Reprint); Tong K Y

CORPORATE SOURCE: HONG KONG POLYTECH UNIV, DEPT ELECT ENGN, HONG KONG, PEOPLES R CHINA (Reprint)

COUNTRY OF AUTHOR: PEOPLES R CHINA

SOURCE: APPLIED SURFACE SCIENCE, (SEP 1998) Vol. 135, No. 1-4, pp. 143-149.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0169-4332.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS; ENGI

LANGUAGE: English

REFERENCE COUNT: 20

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Layered **structures** Si/SiGe were deposited on silicon oxide by RF sputtering system and were furnace crystallised at a temperature of 550 degrees C. The effect of SiGe seeding layer thickness on crystallisation and electrical properties of the top silicon film was studied for SiGe films with thicknesses of **Il**, **22** and 45 nm. Crystallisation process was characterised by scanning electron microscopy (SEM) and **X-ray** diffraction (XRD). Doping of stacked **structures** by phosphorous and boron was investigated through measurement of sheet resistance and Hall mobility. In the scope of investigated thickness ranges, Ii nm thick seeding layer showed the best performance. It is effective in reducing the crystallisation time of the top silicon film, while providing improved morphological and electrical properties of the stacked **structure**.

=> log y

```
=> s interleukin-22 or il-22
L1          47 FILE MEDLINE
L2          90 FILE CAPLUS
L3          60 FILE SCISEARCH
L4          27 FILE LIFESCI
L5          54 FILE BIOSIS
L6          49 FILE EMBASE

TOTAL FOR ALL FILES
L7         327 INTERLEUKIN-22 OR IL-22

=> s l7 and (monomer or dimer)
TOTAL FOR ALL FILES
L14         28 L7 AND (MONOMER OR DIMER)

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15          8 DUP REM L14 (20 DUPLICATES REMOVED)

=> d ibib abs

L15  ANSWER 1 OF 8  LIFESCI    COPYRIGHT 2004 CSA on STN DUPLICATE 1
ACCESSION NUMBER:   2004:26024  LIFESCI
TITLE:              IL-26 Signals through a Novel Receptor Complex Composed of
                    IL-20 Receptor 1 and IL-10 Receptor 2
AUTHOR:             Sheikh, F.; Baurin, V.V.; Lewis-Antes, A.; Shah, N.K.;
                    Smirnov, S.V.; Anantha, S.; Dickensheets, H.; Dumoutier,
                    L.; Renauld, J.-C.; Zdanov, A.; Donnelly, R.P.; Kotenko,
                    S.V.
CORPORATE SOURCE:   Division of Therapeutic Proteins, Center for Biologics
                    Evaluation and Research, Food and Drug Administration,
                    Bethesda, MD 20892
SOURCE:             Journal of Immunology [J. Immunol.], (20040200) vol. 172,
                    no. 4, pp. 2006-2010.
                    ISSN: 0022-1767.
DOCUMENT TYPE:      Journal
FILE SEGMENT:       F
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB   The receptor for IL-26 (AK155), a cytokine of the IL-10 family, has not
     previously been defined. We demonstrate that the active receptor complex
     for IL-26 is a heterodimer composed of two receptor proteins: IL-20R1 and
     IL-10R2. Signaling through the IL-26R results in activation of STAT1 and
     STAT3 which can be blocked by neutralizing Abs against IL-20R1 or IL-10R2.
     IL-10R2 is broadly expressed on a wide variety of tissues, whereas only a
     limited number of tissues express IL-20R1. Therefore, the ability to
     respond to IL-26 is restricted by the expression of IL-20R1. IL-10, IL-19,
     IL-20, IL-22, and IL-24 fail to signal through the
     combination of IL-10R2 and IL-20R1 proteins, demonstrating that this
     receptor combination is unique and specific for IL-26.


=> d ibib abs 2-8

L15  ANSWER 2 OF 8  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
ACCESSION NUMBER:   2004191610  EMBASE
TITLE:              Temporal associations between interleukin
                    22 and the extracellular domains of IL-22R and
                    IL-10R2.
AUTHOR:             Li J.; Tomkinson K.N.; Tan X.-Y.; Wu P.; Yan G.; Spaulding
                    V.; Deng B.; Annis-Freeman B.; Heveron K.; Zollner R.; De
                    Zutter G.; Wright J.F.; Crawford T.K.; Liu W.; Jacobs K.A.;
                    Wolfman N.M.; Ling V.; Pittman D.D.; Veldman G.M.; Fouser
                    L.A.
CORPORATE SOURCE:   L.A. Fouser, Wyeth Research, 87 Cambridge Park Drive,
                    Cambridge, MA 02140, United States. lfouser@wyeth.com
SOURCE:             International Immunopharmacology, (2004) 4/5 (693-708).
                    Refs: 30
                    ISSN: 1567-5769  CODEN: IINMBA
```

PUBLISHER IDENT.: S 1567-5769(04)00015-3
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Interleukin 22** (**IL-22**) is a cytokine induced during both innate and adaptive immune responses. It can effect an acute phase response, implicating a role for **IL-22** in mechanisms of inflammation. **IL-22** requires the presence of the **IL-22** receptor (IL-22R) and IL-10 receptor 2 (IL-10R2) chains, two members of the class II cytokine receptor family (CRF2), to effect signal transduction within a cell. We studied the interaction between human **IL-22** and the extracellular domains (ECD) of its receptor chains in an enzyme-linked immunoabsorbant assay (ELISA)-based format, using biotinylated **IL-22** (bio-**IL-22**) and receptor-fusions containing the ECD of a receptor fused to the Fc of hIgG1 (IL-22R-Fc and IL-10R2-Fc). **IL-22** has measurable affinity for IL-22R-Fc homodimer and undetectable affinity for IL-10R2. **IL-22** has substantially greater affinity for IL-22R/IL-10R2-Fc heterodimers. Further analyses involving sequential additions of receptor homodimers and cytokine indicates that the IL-10R2(ECD) binds to a surface created by the interaction between **IL-22** and the IL-22R(ECD), and thereby further stabilizes the association of **IL-22** within this cytokine-receptor-Fc complex. Both a neutralizing rat monoclonal antibody, specific for human **IL-22**, and human IL-22BP-Fc, an Fc-fusion of the secreted **IL-22** binding-protein and proposed natural antagonist for **IL-22**, bind to similar cytokine epitopes that may overlap the binding site for IL-22R(ECD). Another rat monoclonal antibody, specific for **IL-22**, binds to an epitope that may overlap a separate binding site for IL-10R2(ECD). We propose, based on this data, a temporal model for the development of a functional **IL-22** cytokine-receptor complex.

L15 ANSWER 3 OF 8 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004222746 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15120646
TITLE: Interleukin-26.
AUTHOR: Fickenscher Helmut; Pirzer Heide
CORPORATE SOURCE: Virology Department, Ruprecht Karls University of Heidelberg, Im Neuenheimer Feld 324, D-69120, Heidelberg, Germany.. helmut.fickenscher@med.uni-heidelberg.de
SOURCE: International immunopharmacology, (2004 May) 4 (5) 609-13. Journal code: 100965259. ISSN: 1567-5769.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040505
Last Updated on STN: 20040525
AB Interleukin-26 (IL-26), initially termed AK155, is a cellular sequence homolog to IL-10 belonging to the IL-10 cytokine family. Together with the related genes for interferon-gamma and **IL-22** /IL-TIF, il-26 maps to the human chromosomal region 12q15. The il-26 gene is one of the few differentially expressed genes specifying human T cells after growth-transformation with herpesvirus saimiri, a tumor virus of neo-tropical squirrel monkeys. Only herpesvirus saimiri-transformed T cells have been found to strongly over-express il-26 and to release the protein into the tissue culture supernatant. In a series of other T-cell lines and in native peripheral blood cells, il-26 is transcribed at low levels, but it is not detectable in B cells. Similarly to IL-10, the IL-26 protein forms homo-**dimers**. IL-26 is a candidate to contribute to the transformed phenotype of human T cells after infection by herpesvirus saimiri. Moreover, the T-lymphokine IL-26 is highly likely to play a role in normal and pathological hematology or immunology.

L15 ANSWER 4 OF 8 CAPLUS
ACCESSION NUMBER: 2003:62600 CAPLUS

DOCUMENT NUMBER: 138:220073
TITLE: Crystal structure of interleukin-19 defines a new subfamily of helical cytokines
AUTHOR(S): Chang, Changsoo; Magracheva, Eugenia; Kozlov, Serguei; Fong, Steven; Tobin, Gregory; Kotenko, Sergei; Wlodawer, Alexander; Zdanov, Alexander
CORPORATE SOURCE: NCI-Frederick, Center for Cancer Research, Macromolecular Crystallography Laboratory, Protein Structure Section, National Institutes of Health, Frederick, MD, 21702-1201, USA
SOURCE: Journal of Biological Chemistry (2003), 278(5), 3308-3313
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Interleukin-19 (IL-19) is a novel cytokine that was initially identified during a sequence data base search aimed at finding potential IL-10 homologs. IL-19 shares a receptor complex with IL-20, indicating that the biol. activities of these two cytokines overlap and that both may play an important role in regulating development and proper functioning of the skin. The authors detd. the crystal structure of human recombinant IL-19 and refined it at 1.95-.ANG. resoln. to an R-factor of 0.157. Unlike IL-10, which forms an intercalated **dimer**, the mol. of IL-19 is a **monomer** made of seven amphipathic helixes, A-G, creating a unique helical bundle. On the basis of the obsd. structure, the authors propose that IL-19, IL-20, and other putative members of the proposed IL-10 family together form a distinct subfamily of helical cytokines.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 8 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002376975 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11970958
TITLE: The conserved helix C region in the superfamily of interferon-gamma /interleukin-10-related cytokines corresponds to a high-affinity binding site for the HSP70 chaperone DnaK.
AUTHOR: Vandenbroeck Koen; Alloza Iraide; Brehmer Dirk; Billiau Alfons; Proost Paul; McFerran Neil; Rudiger Stefan; Walker Brian
CORPORATE SOURCE: Biomolecular Sciences Research Group, McClay Research Centre for Pharmaceutical Sciences, Queen's University of Belfast, United Kingdom.. k.vandenbroeck@qub.ac.uk
SOURCE: Journal of biological chemistry, (2002 Jul 12) 277 (28) 25668-76.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020719
Last Updated on STN: 20030105
Entered Medline: 20020812

AB HSP70 chaperones mediate protein folding by ATP-dependent interaction with short linear peptide segments that are exposed on unfolded proteins. The mode of action of the Escherichia coli homolog DnaK is representative of all HSP70 chaperones, including the endoplasmic reticulum variant BiP/GRP78. DnaK has been shown to be effective in assisting refolding of a wide variety of prokaryotic and eukaryotic proteins, including the alpha-helical homodimeric secretory cytokine interferon-gamma (IFN-gamma). We screened solid-phase peptide libraries from human and mouse IFN-gamma to identify DnaK-binding sites. Conserved DnaK-binding sites were identified in the N-terminal half of helix B and in the C-terminal half of helix C, both of which are located at the IFN-gamma **dimer** interface. Soluble peptides derived from helices B and C bound DnaK with high affinity in competition assays. No DnaK-binding sites were found in the loops connecting the alpha-helices. The helix C DnaK-binding site appears to be conserved in most members of the superfamily of interleukin

(IL)-10-related cytokines that comprises, apart from IL-10 and IFN-gamma, a series of recently discovered small secretory proteins, including IL-19, IL-20, **IL-22**/IL-TIF, IL-24/MDA-7 (melanoma differentiation-associated gene), IL-26/AK155, and a number of viral IL-10 homologs. These cytokines belong to a relatively small group of homodimeric proteins with highly interdigitated interfaces that exhibit the strongly hydrophobic character of the interior core of a single-chain folded domain. We propose that binding of DnaK to helix C in the superfamily of IL-10-related cytokines may constitute the hallmark of a novel conserved regulatory mechanism in which HSP70-like chaperones assist in the formation of a hydrophobic dimeric "folding" interface.

L15 ANSWER 6 OF 8 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003008761 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12513909
TITLE: Comparison of **interleukin-22** and interleukin-10 soluble receptor complexes.
AUTHOR: Logsdon Naomi J; Jones Brandi C; Josephson Kristopher; Cook Jennifer; Walter Mark R
CORPORATE SOURCE: Department of Microbiology and Center for Biophysical Sciences and Engineering, University of Alabama at Birmingham, AL 35294, USA.
SOURCE: Journal of interferon & cytokine research : official journal of the International Society for Interferon and Cytokine Research, (2002 Nov) 22 (11) 1099-112.
Journal code: 9507088. ISSN: 1079-9907.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030108
Last Updated on STN: 20030718
Entered Medline: 20030717

AB **Interleukin-22** (**IL-22**) is a cellular homolog of IL-10 that stimulates the production of acute-phase reactants. **IL-22** and IL-10 require different ligand-specific receptor chains (IL-22R and IL-10R1) but share a second receptor chain (IL-10R2) to initiate cellular responses. The quaternary structures and the ability of **IL-22** and IL-10 to engage soluble (s) IL-10R1, IL-22R, IL-10R2 receptor chains were analyzed using size exclusion chromatography and surface plasmon resonance techniques. In contrast to IL-10, which is a homodimer, **IL-22** is a **monomer** in solution that forms a 1:1 interaction with sIL-22R. Kinetic binding data reveal sIL-22R and sIL-10R1 exhibit specific nanomolar binding constants for **IL-22** (k(on)/k(off) = 14.9 nM) and a monomeric isomer of IL-10 (IL-10M1) (k(on)/k(off) = 0.7 nM), respectively. In contrast, IL-10R2 exhibits essentially no affinity for **IL-22** (K(eq) approximately 1 mM) or IL-10M1 (K(eq) approximately 2 mM) alone but displays a substantial increase in affinity for the IL-10/sIL-10R1 (K(eq) approximately 350 microM) and **IL-22**/sIL-22R (K(eq) approximately 45 microM) complexes. Three-dimensional models of **IL-22** and IL-10 receptor complexes suggest two receptor residues (Gly-44 and Arg-96) are largely responsible for the marked differences in ligand affinity observed for sIL-10R1 and sIL-22R vs. sIL-10R2.

L15 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2002422601 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12176383
TITLE: Crystal structure of recombinant human **interleukin-22**.
AUTHOR: Nagem Ronaldo Alves Pinto; Colau Didier; Dumoutier Laure; Renauld Jean-Christophe; Ogata Craig; Polikarpov Igor
CORPORATE SOURCE: Laboratorio Nacional de Luz Sincrotron, Sao Paulo, Brazil.
SOURCE: Structure (Cambridge, Mass. : 2001), (2002 Aug) 10 (8) 1051-62.
Journal code: 101087697. ISSN: 0969-2126.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1M4R
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20020815
Last Updated on STN: 20030305
Entered Medline: 20030304

AB **Interleukin-22** (IL-10-related T cell-derived inducible factor/IL-TIF/**IL-22**) is a novel cytokine belonging to the IL-10 family. Recombinant human **IL-22** (hIL-22) was found to activate the signal transducers and activators of transcription factors 1 and 3 as well as acute phase reactants in several hepatoma cell lines, suggesting its involvement in the inflammatory response. The crystallographic structure of recombinant hIL-22 has been solved at 2.0 A resolution using the SIRAS method. Contrary to IL-10, the hIL-22 **dimer** does not present an interpenetration of the secondary-structure elements belonging to the two distinct polypeptide chains but results from interface interactions between **monomers**. Structural differences between these two cytokines, revealed by the crystallographic studies, clearly indicate that, while a homodimer of IL-10 is required for signaling, hIL-22 most probably interacts with its receptor as a **monomer**.

L15 ANSWER 8 OF 8 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002140993 EMBASE
TITLE: The interleukin-10 family of cytokines.
AUTHOR: Fickenscher H.; Hor S.; Kupers H.; Knappe A.; Wittmann S.; Sticht H.
CORPORATE SOURCE: H. Fickenscher, Hygiene-Institut, Abteilung Virologie, Ruprecht-Karls-Univ. Heidelberg, Im Neuenheimer Feld 324, D-69120 Heidelberg, Germany. helmut_fickenscher@med.uni-heidelberg.de
SOURCE: Trends in Immunology, (1 Feb 2002) 23/2 (89-96).
Refs: 60
ISSN: 1471-4906 CODEN: TIRMAE
PUBLISHER IDENT.: S 1471-4906(01)02149-4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A family of interleukin-10 (IL-10)-related cytokines has emerged, comprising a series of herpesviral and poxviral members and several cellular sequence paralogs, including IL-19, IL-20, **IL-22** [IL-10-related T-cell-derived inducible factor (IL-TIF)], IL-24 [melanoma differentiation-associated antigen 7 (MDA-7)] and IL-26 (AK155). Although the predicted helical structure of these homodimeric molecules is conserved, certain receptor-binding residues are variable and define the interaction with specific heterodimers of different type-2 cytokine receptors. This leads, through the activation of signal transducer and activator of transcription (STAT) factors, to diverse biological effects. For example, whereas IL-10 is a well-studied pleiotropic immunosuppressive and immunostimulatory cytokine, **IL-22**/IL-TIF mediates acute-phase response signals in hepatocytes and IL-20 induces the hyperproliferation of keratinocytes, which has been proposed as a pathogenic mechanism of psoriasis.

=> log y